Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-32 (canceled)

Claim 33 (currently amended): A method of determining whether a chemical agent is a direct inhibitor or activator of an enzyme in a cell whose production by that cell evokes a responsive change in a phenotypic characteristic of the cell, other than the level of said enzyme in said cell per se, which comprises:

(a) providing a first mammalian cell line which produces said enzyme and exhibits said phenotypic response to the enzyme and wherein the level of the enzyme in the cell is maintained such that the cell is capable of exhibiting the phenotypic response following removal of a direct activator or inhibitor of the enzyme;

(b) providing a second mammalian cell line which is alike to the first mammalian cell line, but which produces the enzyme at a lower level than the first cell line, or does not produce the enzyme at all, and which exhibits said phenotypic response to the enzyme to a lesser degree or not at all;

(c) incubating the chemical agent with the first and second cell lines; and

(d) comparing the phenotypic response of the first cell line to the chemical agent with the phenotypic response of the second cell line to the chemical agent~~; and~~

~~(e) determining through the use of a binding assay that the chemical agent binds to the enzyme~~.

Claim 34 (previously presented): The method of Claim 33 wherein said first cell line is obtained by introducing a gene encoding said enzyme into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

Claim 35 (canceled)

Claim 36 (previously presented): The method of either Claim 33 or Claim 34 wherein said chemical agent is a suspected inhibitor of the biological activity of said enzyme.

Claim 37 (previously presented): The method of either Claim 33 or Claim 34 wherein said chemical agent is a suspected activator of the biological activity of said enzyme.

Claims 38-42 (canceled)

Claim 43 (currently amended): A method of determining whether a chemical agent is a direct inhibitor or activator of an enzyme in a cell which comprises:

(a) providing a mammalian test cell which overproduces a selected enzyme relative to a mammalian control cell which is alike to the test cell, but which produces said enzyme at a lower level or essentially does not produce the enzyme, and wherein production of said enzyme in said test cell evokes a responsive change in a phenotypic characteristic of said test cell, other than the level of said enzyme in said test cell per se, which is comparatively greater than in said control cell, and wherein the level of the enzyme in the cell is maintained such that the cell is capable of exhibiting the phenotypic response following removal of a direct activator or inhibitor of the enzyme;

(b) treating said test cell containing the overproduced selected enzyme with said chemical agent; and

(c) examining the treated test cell to determine whether it exhibits a change in said phenotypic characteristic in response to said chemical agent~~; and~~

~~(d) determining through the use of a binding assay that the chemical agent binds to the enzyme~~.

Claim 44 (previously presented): The method of Claim 43 wherein said test cell is obtained by introducing a gene encoding said enzyme into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

Claim 45 (previously presented): The method of Claim 44 wherein the gene is introduced into said host cell by means of a first genetic vector into which the gene has been inserted, and said control cell is obtained by introducing into a similar host cell a second

genetic vector essentially identical to the first genetic vector except that it does not bear said gene insert.

Claim 46 (previously presented): The method of Claim 43 wherein examination for a change in the phenotypic characteristic in response to said chemical agent includes comparing the response of the treated cell to the response of a comparable untreated test cell.

Claim 47 (previously presented): The method of Claim 43 wherein examination includes comparing the phenotypic response of the treated test cell to that of a comparably treated test cell which does not overproduce the selected enzyme.

Claim 48 (previously presented): The method of Claim 43 wherein examination includes comparing the phenotypic response of the test cell in the presence of said chemical agent with the phenotypic response of a second test cell in the presence of a known inhibitor or activator of the enzyme.

Claim 49 (previously presented): The method of any one of Claims 43-48 wherein said chemical agent is a suspected inhibitor of the biological activity of said enzyme.

Claim 50 (previously presented): The method of any one of Claims 43-48 wherein said chemical agent is a suspected activator of the biological activity of said enzyme.

Claims 51-58 (canceled)

Claim 59 (currently amended): A method of determining whether a chemical agent is a direct inhibitor or activator of an enzyme in a cell whose production by that cell evokes a responsive change in a phenotypic characteristic of the cell, other than the level of the enzyme in said cell per se, which comprises:

(a) providing a first mammalian cell line which produces the enzyme and exhibits the phenotypic response to the enzyme and wherein the level of the enzyme in the cell is maintained such that the cell is capable of exhibiting the phenotypic response following removal of a direct activator or inhibitor of the enzyme, said first cell line obtained by introducing a gene encoding the enzyme into a first host cell by means of a first genetic

vector into which said gene has been inserted, said gene being under the control of a promoter functional in said host cell, whereby said gene is expressed;

(b) providing a second mammalian cell line which is alike to the first mammalian cell line, but which produces the enzyme at a lower level than said first cell line, or does not produce the enzyme at all, and which exhibits the phenotypic response to the enzyme to a lesser degree or not at all, said second cell line obtained by introducing into a second host cell which is alike to the first host cell, a second genetic vector essentially identical to said first genetic vector except that it does not bear said gene insert;

(c) incubating the chemical agent with said first and second cell lines; and

(d) comparing the phenotypic response of said first cell line to the chemical agent with the phenotypic response of said second cell line to the chemical agent~~; and~~

~~(e) determining through the use of a binding assay that the chemical agent binds to the enzyme~~.

Claim 63 (currently amended): A method of determining whether a chemical agent is a direct inhibitor or activator of an enzyme whose production by a cell evokes a responsive change in a phenotypic characteristic, other than the level of the enzyme in the cell per se, which comprises:

(a) providing a first mammalian cell line which produces the enzyme and exhibits the phenotypic response to the enzyme and wherein the level of the enzyme in the cell is maintained such that the cell is capable of exhibiting the phenotypic response following removal of a direct activator or inhibitor of the enzyme, said phenotypic response being a graded cellular response;

(b) providing a second mammalian cell line which is alike to the first mammalian cell line, but which produces the enzyme at a lower level than said first cell line, or does not produce the enzyme at all, and which exhibits the phenotypic response to the enzyme to a lesser degree or not at all;

(c) incubating the chemical agent with said first and second cell lines; and

(d) comparing the graded cellular response of said first cell line to the chemical agent with the phenotypic response of said second cell line to the chemical agent~~; and~~

~~(e) determining through the use of a binding assay that the chemical agent binds to the enzyme.~~

Claim 64 (previously presented): The method of Claim 63 wherein the chemical agent is a suspected inhibitor of the biological activity of the enzyme.

Claim 65 (previously presented): The method of Claim 63 wherein the chemical agent is a suspected activator of the biological activity of the enzyme.

Claims 66-70 (canceled)

Claim 71 (currently amended): A method of determining whether a chemical agent is a direct inhibitor or activator of an enzyme which comprises:

(a) providing a mammalian test cell which overproduces the selected enzyme relative to a mammalian control cell which is alike to the test cell, but which produces the enzyme at a lower level or essentially does not produce the enzyme, and wherein production of the enzyme in said test cell evokes a responsive change in a phenotypic characteristic of said test cell, other than the level of the enzyme in said test cell per se, said responsive change being a graded cellular response, which is comparatively greater than in said control cell, and wherein the level of the enzyme in the cell is maintained such that the cell is capable of exhibiting the phenotypic response following removal of a direct activator or inhibitor of the enzyme;

(b) treating said test cell containing the overproduced selected enzyme with the chemical agent; and

(c) examining said treated test cell to determine whether it exhibits a change in said graded cellular response to the chemical agent~~; and~~

~~(d) determining through the use of a binding assay that the chemical agent binds to the enzyme.~~

Claim 72 (previously presented): The method of Claim 71 wherein said test cell is obtained by introducing a gene encoding the enzyme into a host cell, said gene being under the control of a promoter functional in said host cell, whereby said gene is expressed.

Claim 73 (previously presented): The method of Claim 72 wherein said gene is introduced into said host cell by means of a first genetic vector into which said gene has been inserted, and said control cell is obtained by introducing into a similar host cell a second genetic vector essentially identical to said first genetic vector except that it does not bear said gene insert.

Claim 74 (previously presented): The method of Claim 71 wherein examination for the graded cellular response to the chemical agent includes comparing the response of said treated cell to the response of a comparable untreated cell.

Claim 75 (previously presented): The method of Claim 71 wherein examination includes comparing the graded cellular response of said treated test cell to that of a comparably treated test cell which does not overproduce the selected enzyme.

Claim 76 (previously presented): The method of Claim 71 wherein examination includes comparing the graded cellular response of said test cell to the chemical agent with the phenotypic response of a second test cell to a known inhibitor or activator of the enzyme.

Claim 77 (previously presented): The method of any one of Claims 71 to 76 wherein the chemical agent is a suspected inhibitor of the biological activity of the enzyme.

Claim 78 (previously presented): The method of any one of Claims 71 to 76 wherein the chemical agent is a suspected activator of the biological activity of the enzyme.

Claims 79-86 (canceled)

Claim 87 (currently amended): The method of any <u>one</u> of Claims 33, 44, 59, 63, and 71, wherein the enzyme is selected from the group consisting of protein kinase C, ornithine decarboxylase, cyclic AMP-dependent protein kinase, the protein kinase domain of insulin receptor, the protein kinase domain of epidermal growth factor (EGF) receptor, pp60src and p21ras.

Claim 88 (currently amended): The method of any <u>one</u> of Claims 33, 44, 59, 63, and 71, wherein the responsive change in a phenotypic characteristic is observable upon treatment of the test cell with an activator or inhibitor of the enzyme.

Claim 89 (currently amended): The method of any one of Claims 33, 44, 59, 63, and 71, wherein the responsive change in a phenotypic characteristic includes phosphorylation of an intracellular protein substrate of the enzyme.